

AMENDMENTS TO THE CLAIMS

1. (withdrawn—currently amended): A method of enhancing an immune response in a subject to an antigen, the method comprising administering to a subject ~~an antigen and an effective amount of a tryptanthrin compound, or a pharmaceutically acceptable salt thereof, to enhance the immune response to said antigen~~

an immunogenic pharmaceutical composition comprising the antigen and a tryptanthrin compound adjuvant in an amount effect to provide an enhanced immune response to the antigen relative to the response provided without the tryptanthrin compound adjuvant.

2. (withdrawn): The method of claim 1, wherein the antigen is derived from a bacterial, parasitic, viral, or fungal pathogen.

3. (withdrawn—currently amended): The method of claim 2 wherein the bacterial pathogen is selected from the group consisting of diphtheria, staphylococcus, cholera, tuberculosis, tetanus, streptococcus pneumoniae, ~~streptococcus~~ streptococcus agalactiae, streptococcus pyogenes, pertussis, Neisseria meningitis, Neisseria gonorrhoeae, chlamydia, Helicobacter pylori, and Hemophilus influenza type B.

4. (withdrawn): The method of claim 2 wherein the viral pathogen is selected from the group consisting of viral meningitis, rhinovirus, influenza, respiratory syncytial virus, parainfluenza virus, rotavirus, tick borne encephalitis virus, coronaviridae, rhabdoviridae, VZV, EBV, CMV, HIV, HPV, HSV, HAV, HBV, HCV, and SARS.

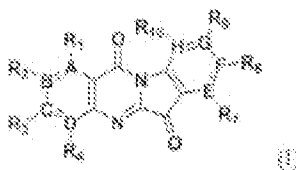
5. (withdrawn): The method of claim 2 wherein the parasitic pathogen is selected from the group consisting of Plasmodium falciparum, Plasmodium ovate, Plasmodium malariae, and P. vivax.

6. (withdrawn): The method of claim 2, wherein the antigen is associated with a disease selected from the group consisting of BCG, cholera, plague, typhoid, hepatitis B infection,

influenza, inactivated polio, rabies, measles, mumps, rubella, oral polio, yellow fever, tetanus, diphtheria, hemophilus influenzae b, meningococcus infection, tick borne encephalitis, SARS, HCV, HIV, and pneumococcus infection.

7. (withdrawn): The method of claim 1 wherein the immune response is the cellular production of one or more cytokines.

8. (withdrawn): The method of claim 1 wherein the tryptanthrin compound is a compound of Formula (I):



wherein

A, B, C, D, E, F, G, and H are independently selected from carbon and nitrogen, or A and B and/or C and D can be taken together to be nitrogen or sulfur; R_1 , R_2 , R_3 , R_4 , R_8 , and R_{10} are independently selected from the group consisting of hydrogen, halogen, loweralkyl, alkyl, substituted alkyl, cycloalkyl, heterocyclyl, alkylheterocyclyl, substituted heterocyclyl, substituted alkenyl, amino, (substituted alkyl)(alkyl)amino, imino, haloloweralkyl, hydroxy, alkoxy, substituted alkoxy, hydroxyalkylthio, nitro, alkylsulfonyl, N-alkylsulfonamide, arylalkyl, arylalkylaryl, arylaryl, aryloxy, arylamino, acylamino, acyloxyamino, alkylaminoacylamino, alkylaminosulfonylamino, alkylamino, alkenylamino, dialkylamino, alkoxyalkylamino, alkoxyalkylheterocyclyl, mercaptoalkoxyalkyl, cyano, formyl, $-COOR_{11}$ wherein R_{11} is hydrogen, loweralkyl, aryl, heterocyclyl, monosaccharide or disaccharide, and $-CONR_{12}R_{13}$ wherein R_{12} and R_{13} are independently selected from hydrogen, loweralkyl, aryl, heterocyclyl, saccharide, peptide and amino acid residues; or R_2 and R_3 taken together form a six membered aromatic ring;

R_7 and R_9 are independently selected from hydrogen, halogen, loweralkyl, haloloweralkyl, cycloalkyl, heterocyclyl, substituted heterocyclyl or heterocyclylalkyl; and

R_1 , R_2 , R_3 , R_4 , R_7 , R_8 , R_9 , and R_{10} are absent when the ring atom to which they would otherwise be bonded is sulfur or double-bonded nitrogen; or

a pharmaceutically acceptable salt,

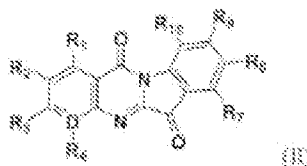
provided that R₁, R₂, R₃, R₄, R₇, R₈, R₉, and R₁₀ are not all hydrogen when A, B, C, D, E, F, and H are carbon.

9. (withdrawn): The method of claim 8,
wherein

A, B, C, D, E, F, G, and H are independently selected from carbon and nitrogen;

R₁, R₂, R₃, R₄, R₈ and R₁₀ are independently selected from the group consisting of hydrogen, halogen, loweralkyl, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, substituted alkenyl, (substituted alkyl)(alkyl)amino, haloloweralkyl, hydroxy, alkoxy, substituted alkoxy, hydroxyalkylthio, nitro, N-alkylsulfonamide, cyano, -COOR₁₁ wherein R₁₁ is hydrogen, loweralkyl, aryl, heterocyclyl, monosaccharide or disaccharide, and -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently selected from hydrogen, loweralkyl, aryl, heterocyclyl, saccharide, peptide and amino acid residues.

10. (withdrawn): The method of claim 1 wherein the tryptanthrin compound is a compound of Formula (II):



wherein

D is carbon or nitrogen, and R₄ is absent when D is N;

R₁ is hydrogen, halogen, or loweralkyl;

R₂ is hydrogen or halogen;

R₃ is hydrogen, halogen, heterocyclyl, substituted heterocyclyl, (substituted alkyl)(alkyl)amino, or hydroxyalkylthio;

R₄ is hydrogen, halogen, alkoxy, substituted alkoxy, or hydroxy;

R₇ is hydrogen or haloloweralkyl;

R₈ is hydrogen, halogen, substituted alkoxy, haloloweralkyl, nitro, N-alkylsulfonamide, substituted alkenyl, substituted alkyl, COOR₁₁ wherein R₁₁ is loweralkyl, or -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently hydrogen or loweralkyl;

R₉ is hydrogen; and

R₁₀ is hydrogen, halogen, or loweralkyl;

or a pharmaceutically acceptable salt thereof.

11. (withdrawn): The method of claim 1, wherein the tryptanthrin compound is selected from the group consisting of:

8-nitroindolo[2,1-b]quinazoline-6,12-dione,

3,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,

10-fluoroindolo[2,1-b]quinazoline-6,12-dione,

1,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,

8-fluoro-1-methylindolo[2,1-b]quinazoline-6,12-dione,

8,10-difluoroindolo[2,1-b]quinazoline-6,12-dione,

2,4-dibromo-1-fluoro-8-iodoindolo[2,1-b]quinazoline-6,12-dione,

2,4-dibromo-1-chloro-8-iodoindolo- [2,1-b]quinazoline-6,12-dione,

2,4-dibromo-1-fluoroindolo[2,1-b]quinazoline-6,12-dione,

8-chloro-2-iodoindolo[2,1-b]quinazoline-6,12-dione,

8-chloro-3-fluoroindolo[2,1-b]quinazoline-6,12-dione,

8-fluoro-4-hydroxyindolo[2,1-b]quinazoline-6,12-dione,

N-ethyl-4-(methoxy)-6,12-dioxo-6,12-dihydroindolo[2,1-b]quinazoline-8-carboxamide,

3-fluoro-8-[(trifluoromethyl)oxy]indolo[2,1-b]quinazoline-6,12-dione,

3-[(2-hydroxyethyl)thio]-8-[(trifluoromethyl)oxy]indolo[2,1-b]quinazoline-6,12-dione,

pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,

9-fluoropyrido[2',3':4,5]pyrimido[1,2-a] indole-5,11-dione,

9-bromopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,

9-chloropyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,

9-iodopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,

ethyl 5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-carboxylate,
N-octyl-5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-sulfonamide,
10-(trifluoromethyl)pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
(5E)-6-(5,11-dioxo-5,11 dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hex-5-enyl
acetate,
6-(5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hexyl dihydrogen
phosphate, and
9-[(trifluoromethyl)oxy]pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
or a pharmaceutically acceptable salt thereof.

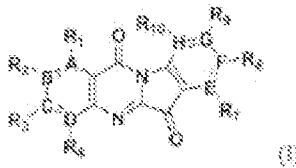
12. (currently amended): An immunogenic pharmaceutical composition ~~for enhancing an immune response in a subject to an antigen~~, comprising ~~the antigen~~ an antigen and ~~an effective amount of a tryptanthrin compound adjuvant, said tryptanthrin compound adjuvant providing in an amount effective to provide~~ an enhanced immune response to the antigen ~~[[than]]~~ relative to the response provided without the tryptanthrin compound adjuvant, and wherein said antigen is not BCG.

13. (original): The composition of claim 12, further comprising an aqueous carrier.

14. (previously presented): The composition of claim 12, wherein the antigen is associated with a disease selected from the group consisting of cholera, plague, typhoid, hepatitis B infection, influenza, inactivated polio, rabies, measles, mumps, rubella, oral polio, yellow fever, tetanus, diphtheria, hemophilus influenzae b, meningococcus infection, tick borne encephalitis, SARS, HCV, HIV, and pneumococcus infection.

15. (previously presented): The composition of claim 12, wherein the tryptanthrin compound enhances an immune response to the antigen and the immune response is the cellular production of one or more cytokines.

16. (original): The composition of claim 12, wherein the tryptanthrin compound is a compound of Formula I:



wherein

A, B, C, D, E, F, G, and H are independently selected from carbon and nitrogen, or A and B and/or C and D can be taken together to be nitrogen or sulfur;

R₁, R₂, R₃, R₄, R₈, and R₁₀ are independently selected from the group consisting of hydrogen, halogen, loweralkyl, alkyl, substituted alkyl, cycloalkyl, heterocyclyl, alkylheterocyclyl, substituted heterocyclyl, substituted alkenyl, amino, (substituted alkyl)(alkyl)amino, imino, haloloweralkyl, hydroxy, alkoxy, substituted alkoxy, hydroxyalkylthio, nitro, alkylsulfonyl, N-alkylsulfonamide, arylalkyl, arylalkylaryl, arylaryl, aryloxy, arylamino, acylamino, acyloxyamino, alkylaminoacylamino, alkylaminosulfonylamino, alkylamino, alkenylamino, dialkylamino, alkoxyalkylamino, alkoxyalkylheterocyclyl, mercaptoalkoxyalkyl, cyano, formyl, -COOR₁₁ wherein R₁₁ is hydrogen, loweralkyl, aryl, heterocyclyl, monosaccharide or disaccharide, and -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently selected from hydrogen, loweralkyl, aryl, heterocyclyl, saccharide, peptide and amino acid residues; or R₂ and R₃ taken together form a six membered aromatic ring;

R₇ and R₉ are independently selected from hydrogen, halogen, loweralkyl, haloloweralkyl, cycloalkyl, heterocyclyl, substituted heterocyclyl or heterocyclylalkyl; and

R₁, R₂, R₃, R₄, R₇, R₈, R₉, and R₁₀ are absent when the ring atom to which they would otherwise be bonded is sulfur or double-bonded nitrogen; or

a pharmaceutically acceptable salt thereof,

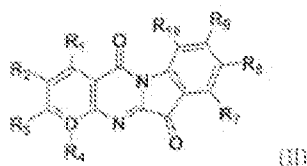
provided that R₁, R₂, R₃, R₄, R₇, R₈, R₉, and R₁₀ are not all hydrogen when A, B, C, D, E, F, and H are carbon.

17. (original): The composition of claim 16,
wherein

A, B, C, D, E, F, G, and H are independently selected from carbon and nitrogen;

R₁, R₂, R₃, R₄, R₈ and R₁₀ are independently selected from the group consisting of hydrogen, halogen, loweralkyl, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, substituted alkenyl, (substituted alkyl)(alkyl)amino, haloloweralkyl, hydroxy, alkoxy, substituted alkoxy, hydroxyalkylthio, nitro, N-alkylsulfonamide, cyano, -COOR₁₁ wherein R₁₁ is hydrogen, loweralkyl, aryl, heterocyclyl, monosaccharide or disaccharide, and -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently selected from hydrogen, loweralkyl, aryl, heterocyclyl, saccharide, peptide and amino acid residues.

18. (withdrawn): The composition of claim 12, wherein the tryptanthrin compound is a compound of Formula II:



wherein

D is carbon or nitrogen, and R₄ is absent when D is N;

R₁ is hydrogen, halogen, or loweralkyl;

R₂ is hydrogen or halogen;

R₃ is hydrogen, halogen, heterocyclyl, substituted heterocyclyl, (substituted alkyl)(alkyl)amino, or hydroxyalkylthio;

R₄ is hydrogen, halogen, alkoxy, substituted alkoxy, or hydroxy;

R₇ is hydrogen or haloloweralkyl;

R₈ is hydrogen, halogen, substituted alkoxy, haloloweralkyl, nitro, N-alkylsulfonamide, substituted alkenyl, substituted alkyl, COOR₁₁ wherein R₁₁ is loweralkyl, or -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently hydrogen or loweralkyl;

R₉ is hydrogen; and

R₁₀ is hydrogen, halogen, or loweralkyl;

or a pharmaceutically acceptable salt thereof.

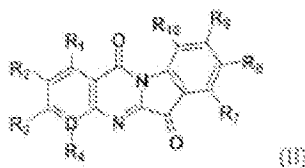
19. (original): The composition of claim 12, wherein the tryptanthrin compound is selected from the group consisting of

8-nitroindolo[2,1-b]quinazoline-6,12-dione,
 3,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,
 10-fluoroindolo[2,1-b]quinazoline-6,12-dione,
 1,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,
 8-fluoro-1-methylindolo[2,1-b]quinazoline-6,12-dione,
 8,10-difluoroindolo[2,1-b]quinazoline-6,12-dione,
 2,4-dibromo-1-fluoro-8-iodoindolo[2,1-b]quinazoline-6,12-dione,
 2,4-dibromo-1-chloro-8-iodoindolo[2,1-b]quinazoline-6,12-dione,
 2,4-dibromo-1-fluoroindolo[2,1-b]quinazoline-6,12-dione,
 8-chloro-2-iodoindolo[2,1-b]quinazoline-6,12-dione,
 8-chloro-3-fluoroindolo[2,1-b]quinazoline-6,12-dione,
 8-fluoro-4-hydroxyindolo[2,1-b]quinazoline-6,12-dione,
 N-ethyl-4-(methyloxy)-6,12-dioxo-6,12-dihydroindolo[2,1-b]quinazoline-8-carboxamide,
 3-fluoro-8-[(trifluoromethyl)oxy]indolo[2,1-b]quinazoline-6, 12-dione,
 3-[(2-hydroxyethyl)thio]-8-[(tri fluoromethyl)oxy]indolo[2,1-b]quinazoline-6,12-dione,
 pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 9-fluoropyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 9-bromopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 9-chloropyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 9-iodopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 ethyl 5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-carboxylate,
 N-octyl-5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-sulfonamide,
 10-(trifluoromethyl)pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
 (5E)-6-(5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hex-5-enyl acetate,
 6-(5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hexyl dihydrogen phosphate, and

9-[(trifluoromethyl)oxy]pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
or a pharmaceutically acceptable salt thereof.

20. (withdrawn): A method of immunotherapy for the treatment of cancer, the method comprising administering to a subject an immunostimulatory effective amount of a tryptanthrin derivative.

21. (withdrawn): The method of claim 20, wherein the tryptanthrin derivative is a compound of Formula II:



wherein

D is carbon or nitrogen, and R₄ is absent when D is N;

R₁ is hydrogen, halogen, or loweralkyl;

R₂ is hydrogen or halogen;

R₃ is hydrogen, halogen, heterocyclyl, substituted heterocyclyl, (substituted alkyl)(alkyl)amino, or hydroxyalkylthio;

R₄ is hydrogen, halogen, alkoxy, substituted alkoxy, or hydroxy;

R₇ is hydrogen or haloloweralkyl;

R₈ is hydrogen, halogen, substituted alkoxy, haloloweralkyl, nitro, N-alkylsulfonamide, substituted alkenyl, substituted alkyl, COOR₁₁, wherein R₁₁ is loweralkyl, or -CONR₁₂R₁₃ wherein R₁₂ and R₁₃ are independently hydrogen or loweralkyl;

R₉ is hydrogen; and

R₁₀ is hydrogen, halogen, or loweralkyl;

or a pharmaceutically acceptable salt thereof.

22. (withdrawn): The method of claim 20, wherein the tryptanthrin derivative is selected from the group consisting of

8-nitroindolo[2,1-b]quinazoline-6,12-dione,
3,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,
10-fluoroindolo[2,1-b]quinazoline-6,12-dione,
1,8-difluoroindolo[2,1-b]quinazoline-6,12-dione,
8-fluoro-1-methylindolo[2,1-b]quinazoline-6,12-dione,
8,10-difluoroindolo[2,1-b]quinazoline-6,12-dione,
2,4-dibromo-1-fluoro-8-iodoindolo[2,1-b]quinazoline-6,12-dione,
2,4-dibromo-1-chloro-8-iodoindolo[2,1-b]quinazoline-6,12-dione,
2,4-dibromo-1-fluoroindolo[2,1-b]quinazoline-6,12-dione,
8-chloro-2-iodoindolo[2,1-b]quinazoline-6,12-dione,
8-chloro-3-fluoroindolo[2,1-b]quinazoline-6,12-dione,
8-fluoro-4-hydroxyindolo[2,1-b]quinazoline-6,12-dione,
N-ethyl-4-(methyloxy)-6,12-dioxo-6,12-dihydroindolo[2,1-b]quinazoline-8-carboxamide,
3-fluoro-8-[(trifluoromethyl)oxy]indolo[2,1-b]quinazoline-6,12-dione,
3-[(2-hydroxyethyl)thio]-8-[(trifluoromethyl)oxy]indolo[2,1-b]quinazoline-6,12-dione,
pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
9-fluoropyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
9-bromopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
9-chloropyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
9-iodopyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
ethyl 5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-carboxylate,
N-octyl-5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indole-9-sulfonamide,
10-(trifluoromethyl)pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
(5E)-6-(5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hex-5-enyl
acetate,
6-(5,11-dioxo-5,11-dihydropyrido[2',3':4,5]pyrimido[1,2-a]indol-9-yl)hexyl dihydrogen
phosphate, and
9-[(trifluoromethyl)oxy]pyrido[2',3':4,5]pyrimido[1,2-a]indole-5,11-dione,
or a pharmaceutically acceptable salt thereof.

23.-31. (canceled)